

## REMARKS

Claims 1, 2, 10, 25, and 26 are in the application. No claim is allowed.

Claims 25 and 26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,586, 406 in view of Atkinson, et al., of record. This rejection is respectfully traversed. The claims in the '406 patent require the presence of GDF-5. The disclosure and claims in Atkinson, et al. require the presence of mixtures of transforming growth factor- $\beta$  super family proteins and bone matrix proteins, and FGF-I, in addition to a repair matrix. The present claims call for a matrix comprising collagen I or collagen II and an effective amount only of BMP-4 sufficient to induce chondrogenesis. Therefore, not only is there a differentiation of scope of the present claims from those in the '406 patent, but also the teachings of Atkinson, et al. teach away from the present invention. Atkinson, et al. teach a composition requiring a mixture of proteins, including at least two different TGF- $\beta$  super family proteins, and at least one bone matrix protein or at least one growth factor protein. See, for example, column 9, lines 19-31. It is therefore submitted that it is unobvious to form a chondrogenesis-inducing composition which consists only of the matrix and a single TGF- $\beta$  super family protein, BMP 4.

Claims 25 and 26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, and 6-9 of co-pending SN 10/444,640 in view of Atkinson, et al. The present claims exclude the presence of GDF-5 therefore there is clearly a demarcation of scope between the claims of the co-pending application and the present claims. Again, as discussed above, Atkinson, et al. require a mixture of TGF- $\beta$  proteins as well as one bone matrix protein or at least one growth factor protein. There is no teaching in Atkinson, et al. that only a single TGF- $\beta$  super family protein would be sufficient to induce chondrogenesis, much less that the protein could be BMP-4. Accordingly, it is respectfully submitted that the present claims are unobvious over the combination of the co-pending application and Atkinson, et al. and withdrawal of the provisional rejection is requested.

Claims 1, 2, 10, 25, and 26 are rejected under 35 U.S.C. 112, second paragraph. This rejection is now moot since the objectionable phrase has been deleted from the claims.

Claims 1, 2, 10, 25 and 26 are rejected under 35 U.S.C 102(e) as allegedly being anticipated by Atkinson, et al. This rejection is respectfully traversed. As discussed above, Atkinson, et al. require in their composition at least two different TGF- $\beta$  superfamily proteins, at least one bone matrix protein or at least one growth factor protein. Therefore the minimum number of active proteins present in the composition of Atkinson, et al. is three. Other than the matrix itself, the composition used in the claimed method calls only for the presence of BMP 4. Accordingly, Atkinson, et al. does not anticipate the present invention.

Claims 2, 10, and 25 are rejected under 35 U.S.C. 102(e) as anticipated by Radice, et al., U.S. Patent No. 6,699,471. This rejection is respectfully traversed. Radice, et al. do not use an extracellular collagen I or collagen II-containing matrix to culture the chondrogenic cells. In the passage cited by the Examiner in columns 13 and 14, the chondrogenic cells are first denuded from native tissue, then added to a cell culture plate deprived of an anchorage. See column 14, lines 41-43. This allows the cells to interact with one another and coalesce to generate a cohesive plug of cells. Then, as the cells are cultured and begin to differentiate the cells themselves produce and secrete markers such as type II collagen and sulfated proteoglycans. See column 14, lines 43-46. It is this cartilage patch grown in the culture plate that is used.

According to the present invention the chondrocytes are added to an extracellular matrix which is already existing, and to an effective amount of BMP-4. Then the chondrocytes are cultured *in vitro* in that matrix. The matrix provides a support for in growth of the chondrocytes. This is again in contrast to Radice, et al. who use unanchored cells. See column 14, lines 41-42. Then the extracellular matrix, along with the cells grown on and into the matrix according to the invention, is implanted. Accordingly, Radice, et al. disclose a quite different process from the present invention and do not anticipate the invention.

Claims 25 and 26 are rejected under 35 U.S.C. 103(a) as allegedly being obvious over Heidaran, et al., U.S. 6,586,406, in view of Atkinson, et al. of record. Withdrawal of this rejection is requested. Heidaran, et al. is not a competent reference against the present application. The present application was filed after November 29, 1999. Accordingly, Heidaran, et al. is disqualified as prior art against the claimed invention if the subject matter of Heidaran, et al. and the present claimed invention were at the time the present invention was made owned by the same person or subject to an obligation of assignment to the same person. Accompanying

this response and attached on a separate page is a statement to that effect by the undersigned.  
Accordingly, Heidaran, et al. is not a reference and this rejection should be withdrawn.

**STATEMENT OF COMMON OWNERSHIP**

The undersigned representative of record of the application serial number 09/805,816 states that the application and U.S. Patent No. 6,586,406 were at the time the invention of application 09/805,816 was made, owned by Orquest, Inc. The application and the patent were subsequently simultaneously assigned to DePuy Acromed, Inc.

For the foregoing reasons it is submitted that the application is in condition for allowance and a prompt passage to is respectfully requested.

Respectfully submitted,

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